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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/082,659	02/25/2002	Maurice Cohen	6171.US.D2	6272

23492 7590 08/12/2003

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EXAMINER	
HARRIS, ALANA M	

ART UNIT	PAPER NUMBER
1642	8

DATE MAILED: 08/12/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/082,659	Applicant(s) COHEN ET AL.	
	Examiner Alana M. Harris, Ph.D.	Art Unit 1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group IV (claims 1-4) in Paper No. 7, received May 27, 2003 is acknowledged.

2. Claims 1-9 are pending.

Claims 5-9, drawn to non-elected inventions are withdrawn from examination.

Claims 1-4 are examined on the merits.

Information Disclosure Statement

3. The information disclosure statement filed June 27, 2002 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because the listed references, C1-C10 did not accompany the application. It has been placed in the application file, but the information referred to therein has not been considered as to the merits. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609 ¶ C(1).

Specification

4. The disclosure is objected to because of the following informalities:

(a) on page 50, lines 3 and 9 there is missing text, i.e. American Type Culture Collection (ATCC) deposit number and a date;

(b) the address of ATCC should be updated;

and (c) the specification references Figures, however there are no references in the specification as noted in the preliminary amendment received April 12, 2002.

Correction is required.

Claim Objections

5. Claim 1 is objected to because of the following informality: it references non-elected subject matter, SEQ ID NO: 1-3. Correction is required.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-4 are drawn to "[a] purified polynucleotide or fragment thereof derived from a PS190 gene, wherein the said polynucleotide capable of selectively hybridizing

to the nucleic acid of said PS190 gene and has at least 50% identity to a sequence... consisting of ...SEQ ID NO: 4, and fragments or complements thereof" in order to detect prostate cancer. PS190 has been identified in the specification as SEQ ID NO: 4, a nucleic acid sequence. The generic claim language of claim 1 does not adequately define: (a) species of fragments or complements of SEQ ID NO: 4, (b) nucleic acids that selectively hybridize to a PS190 defined as SEQ ID NO: 4, and (c) nucleic acids that have at least 50% identity to a sequence from SEQ ID NO: 4 that fall within the realm of the claim. Accordingly, one of skill in the art cannot ready envisage the identity of the members of the genera. The written description in this case only sets forth the nucleic acid sequence recognized as SEQ ID NO: 4 and not any and all possible nucleic acid sequences comprising fragments, complements, variants and undefined nucleic acids that may hybridize to SEQ ID NO: 4. As the claims read they encompass variants and undefined fragments and complements of PS190. Furthermore, the polynucleotides have not been clearly identified by the acronym, PS190. Applicants are not in possession of all polynucleotides derived from a PS190 gene. The written description in this case only sets forth one PS190 nucleic acid molecule identified as SEQ ID NO: 4.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that

[he or she] invented what is claimed." (*See Vas-Cath* at page 1116). Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

Applicants are not required to disclose every species encompassed by a genus. For example as indicated in *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

Applicants are not entitled, nor is the specification enabled for the use of all polynucleotides, fragments, complements thereof and nucleic acid capable of binding SEQ ID NO: 4. Applicants are only in possession of 1 species of the PS190 gene, which has not defined by structure. Applicants are not permitted to claim all nucleic acids that are encompassed by the claim language of the claims and hence not entitled to the wide breadth of the claims at issue. There is no description and no information regarding the relation of structure to function. Structural features that could distinguish the compounds in the genus from others are excluded and missing from the disclosure.

This is insufficient to support the generic claims as provided by the Interim Written Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645.

8. Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 1-4 are broadly drawn to polynucleotides, fragments and complements of SEQ ID NO: 4, as well as nucleic acids that selectively hybridize to SEQ ID NO:4 which are to be used in methods of detecting a target polynucleotide or mRNA within a test sample (such as blood, urine, saliva and stool) in order to assess whether or not the test sample contains a polynucleotide indicative of prostate cancer, see page 57, lines 9-13; page 59, lines 30-34; and page 80, lines 1-10. These diagnostic methods include for example hybridization techniques, polymerase chain reaction, as well as reverse transcription polymerase chain reaction.

The specification asserts that the ESTs corresponding to the consensus sequence SEQ ID NO: 4 (or fragments thereof) were not found in any (0 of 399) of the other, non-prostate, libraries of the data base.", see page 50, lines 31-35. This result is not indicative of prostate cancer, but instead of specific tissue typing. Even if tissue typing was considered to be a valid utility the specification is not enabled. The specification does not enable one of ordinary skill in the art to definitively assess the incidence of any type of cancer, particularly prostate cancer in a test sample. And while the evidence presented in the specification does point to the high occurrence of PS190 nucleotides and SEQ ID NO: 4 in prostate tissues, this is not sufficient in implementing said sequences in a molecular based diagnostic method for prostate cancer.

Furthermore, Applicants have not provided any disclosure enabling the use of fragments, complements and nucleic acids that selectively hybridize to SEQ ID NO: 4. There is no disclosure designating which fragments or what criteria is used for discerning which hybridized nucleic acids would be effective in any diagnostic method. The experimental design presented in the specification lacks information regarding the applicability of SEQ ID NO: 4 and fragments, complements and sequences thereof in diagnostic methods relative to prostate diseases.

Applicants have not set forth any supporting evidence that suggests that any of SEQ ID NO: 4 or fragments, complements, thereof are unique tumor or molecular markers for prostate cancer. Similarly, the test samples to be used in the methods do not encompass sources from pancreatic tissue itself. In addition, the molecular-based techniques presented in the specification do not take into account the possibility that results from such diagnostic tests can be obscured by the presence of excess normal DNA. Tascilar et al. (Annals of Oncology 10,Suppl. 4:S107-S110, 1999) reviewed the role of tumor markers in the diagnosis of pancreatic cancer. And even though this organ is distinct from the prostate the observations are relevant and applicable to this instant case. It is art known that molecular–based assays are valid tools used in predicting and detecting diseases, however "...these tests should be interpreted with caution..." and "the genetic changes found in sources other than the pancreas itself (blood, stool) should be evaluated prudently".

Based on the analysis set forth it would require undue experimentation for the skilled artisan to practice this invention because there is no support in the specification

for the enablement of the broadly claimed invention. Therefore, in view of the insufficient guidance in the specification, extensive experimentation would be required to enable the claims.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1-4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claim 1 is vague and indefinite in the recitation "capable of selectively hybridizing to the nucleic acid". The metes and bounds are unclear in the absence of limitations specifying specific stringency conditions.

b. The recitation "polynucleotide or fragment derived from a PS190 gene" in claim 1 is vague and indefinite. It is not clear how a polynucleotide is derived, i.e. the sequence has been altered, residues mutated. Accordingly, the metes and bounds cannot be determined.

Claim Rejections - 35 USC § 101

11. Claims 1-4 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific, substantial, credible or asserted utility or a well established utility.

Claims 1-4 are broadly drawn to "[a] purified polynucleotide or fragment thereof derived from a PS190 gene, wherein the said polynucleotide capable of selectively

hybridizing to the nucleic acid of said PS190 gene and has at least 50% identity to a sequence... consisting of ...SEQ ID NO: 4, and fragments or complements thereof", as well as methods of producing the polynucleotide, which comprises a sequence encoding at least one PS190 epitope. According to the specification these nucleic acid sequences are useful for detecting a target polynucleotide or mRNA within a test sample in order to assess whether or not the test sample contains a polynucleotide indicative of prostate cancer, see bridging paragraph of pages 3 and 4. These diagnostic methods include for example hybridization techniques, ligase chain reaction (LCR), polymerase chain reaction, as well as reverse transcription polymerase chain reaction. The specification also contemplates the use of these methods for diagnosing, staging, monitoring, prognosticating or determining predisposition to diseases or conditions of the prostate, see page 1, lines 6-11. Applicants have disclosed in the specification that "[expressed sequence tags (ESTs)] corresponding to the consensus sequences of PS190 were found in 25% ...of prostate tissue libraries" and "ESTs corresponding to the consensus sequence SEQ ID NO: 4 (or fragments thereof) were not found in any (0 of 399) of the other, non-prostate, libraries of the data base.", see page 50, lines 31-35. This result does not support Applicants' asserted use of the claimed polynucleotides (inclusive of undefined sequences) for detection of any prostate disorders, particularly prostate cancer. There is no disclosure or working examples that demonstrate the specifically asserted utility and evidences a substantial utility was well established at the time of filing. Applicants have provided information that simply supports the fact that SEQ ID NO: 4 may be expressed especially in prostate tissues

versus non-prostate tissues. There is no information supporting the use of SEQ ID NO: 4, nor fragments, variants, complements, or sequences that selectively hybridize as a specific tumor marker to be implemented in methods listed in the specification. The specification does not exemplify the use of any of the said sequences in differential expression in normal prostate tissue versus high risk (potentially diseased) prostate tissue or their reliability as biomarkers, which may signal a stage of carcinogenesis. Based on the analysis set forth above the specification does not exemplify sufficient findings that constitute a specific, substantial or credible utility.

Claims 1-4 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by a specific, substantial or credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (703) 306-5880. The examiner can normally be reached on 7:00 am to 4:30 pm, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, Ph.D. can be reached on (703) 308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4315 for regular communications and (703) 308-4315 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Alana M. Harris, Ph.D.
August 11, 2003